

1. IDENTIFICATION

Product identifier: Tretinoin Gel, 0.025%, 0.01%

Synonyms: 4Z8, 8F8, 3W7, 7U8

Manufacturer Name: Perrigo Company.
Address: 515 Eastern Avenue
 Allegan, MI 49010 USA

Telephone number: 269-673-8451

Emergency phone number: 888-464-2986 (U.S. calls)
 +1 760-476-3962 Code 333304 (International calls)

Email Address: SDSRequest@perrigo.com

Recommended use: Human drug – for treatment of acne vulgaris - for prescription use only.

Restrictions on use: For external use only. Use only as directed.

2. HAZARD(S) IDENTIFICATION

Classification:

Physical	Health
Flammable Liquid Category 3	Eye Irritant Category 2A Reproductive Toxicity Category 1B

Label Elements:
Danger!



Hazard statement(s)

Highly flammable liquid and vapor
 Causes serious eye irritation.
 May damage fertility or the unborn child.
Precautionary statement(s)
 Obtain special instructions before use.
 Do not handle until all safety precautions have been read and understood.
 Keep away from heat, sparks, open flames and hot surfaces. No smoking.
 Keep container tightly closed.
 Ground and bond container and receiving equipment.
 Use explosion-proof electrical, ventilating and lighting equipment.

Precautionary statement(s)

Use only non-sparking tools.
 Take precautionary measures against static discharge.
 Wash hands thoroughly after handling.
 Wear protective gloves and eye protection.
 IF IN EYES: Rinse cautiously with water for several minutes.
 Remove contact lenses, if present and easy to do. Continue rinsing. If eye irritation persists: Get medical attention.
 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water.
 IF exposed or concerned: Get medical attention.
 In case of fire: Use water spray, carbon dioxide or alcohol-resistant foam to extinguish.
 Store in a well-ventilated place. Keep cool. Store locked up.
 Dispose in accordance with local and national regulations.

3. COMPOSITION / INFORMATION ON INGREDIENTS

Chemical name	CAS No.	Concentration
Tretinoin	302-79-4	0.025-0.01%
Ethanol	64-17-5	Proprietary
Hydroxypropyl Cellulose	9004-64-2	Proprietary

The exact percentage (concentration) of composition has been withheld as a trade secret.

4. FIRST-AID MEASURES

Inhalation: Remove person to fresh air. If irritation occurs or symptoms develop, get medical attention.

Skin contact: For unintended skin contact immediately remove contaminated clothing. Wash skin thoroughly with soap and water for several minutes. If irritation or other symptoms develop, get immediate medical attention. Launder clothing before reuse.

Eye contact: Immediately flush eyes with water while lifting the upper and lower lids. Get medical attention if irritation persists.

Ingestion: Rinse mouth with water. Do not induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to a person who is unconscious or convulsing. Get immediate medical attention.

Most important symptoms/effects, acute and delayed: May cause eye irritation. Swallowing may cause nervous system and gastrointestinal effects. Inhalation of ethanol vapors may cause dizziness and drowsiness. May cause adverse effects on the unborn child.

Indication of immediate medical attention and special treatment, if necessary: Immediate medical attention is not generally required.

5. FIRE-FIGHTING MEASURES

Extinguishing media: Use water fog or spray, carbon dioxide, dry chemical or alcohol-resistant foam.

Specific hazards arising from the chemical: Flammable liquid and vapor. Vapors are heavier than air and can flow to remote ignition sources and flash back. Vapors may be explosive in confined areas. Vapors will collect in low areas. Vapors may be ignited by static sparks. Flames may be invisible in daylight.

Special protective equipment and precautions for fire-fighters: Firefighters should wear positive pressure self-contained breathing apparatus and full protective clothing for all fires involving chemicals. Cool fire exposed containers with water.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment, and emergency procedures: Wear appropriate protective clothing and equipment as described in Section 8. Eliminate all ignition sources and ventilate the area with explosion-proof equipment. Prevent entry into basements or confined areas.

Environmental Precautions: Prevent spill from entering sewers and water courses. Report releases as required by local and national authorities.

Methods and materials for containment and cleaning up: Stop spill at the source if it is safe to do so. Absorb with an inert material. Use non-sparking tools and equipment. Collect into a suitable container for disposal.

7. HANDLING AND STORAGE

Precautions for safe handling: Avoid eye contact. Avoid breathing vapors. Use only with adequate ventilation. Wash thoroughly after handling. Remove contaminated clothing and launder before re-use. Keep product away from heat, sparks and all other sources of ignition. Electrically bond and ground transfer equipment, Use appropriately rated electrical equipment in areas where this material is handled and stored. Keep containers closed when not in use.

Conditions for safe storage, including any incompatibilities: Store as indicated on product packaging. Protect containers from physical damage. Store in a cool area. Keep away from excessive heat and open flames. Keep containers closed when not in use. Store away from oxidizers.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Exposure guidelines:

Tretinoin	PERRIGO OEB4 (1-10 ug/m3)
Ethanol	1000 ppm TWA OSHA PEL 1000 ppm STEL ACGIH TLV
Hydroxypropyl Cellulose	None Established

Appropriate engineering controls: Use with adequate general or local exhaust ventilation to minimize exposures levels. Use explosion-proof equipment where required.

Individual protection measures:

Respiratory protection: None needed under normal use conditions. If exposure levels are excessive and irritation is experienced, a NIOSH approved organic vapor or supplied air respirator is recommended. Selection of respiratory protection depends on the contaminant type, form and concentration. Select in accordance with OSHA 1910.134 and good Industrial Hygiene practice.

Skin protection: Impervious gloves recommended for other than use.

Eye protection: Chemical safety goggles recommended if contact with the drug product is possible.

Other: None known.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance (physical state, color, etc.): Pale yellow liquid

Odor: Alcohol odor

Odor threshold: 100 ppm (Ethanol)	pH: Not determined
Melting point/freezing point: Not determined	Boiling Point: Not determined
Flash point: 20°C (68°F) (Closed Cup)	Evaporation rate: Not determined
Flammability (solid, gas): Not applicable	VOC: Not determined
Flammable limits: LEL: 3%	UEL: 19%
Vapor pressure: 59.3 mmHg @ 25°C (ethanol)	Vapor density: 1.59 (ethanol)
Relative density: 0.82	Solubility(ies): Soluble
Partition coefficient: n-octanol/water: Not available	Auto-ignition temperature: Not determined
Decomposition temperature: Not available	Viscosity: Not determined

10. STABILITY AND REACTIVITY

Reactivity: Not reactive under normal conditions of use.

Chemical stability: Stable.

Possibility of hazardous reactions: Reaction with strong oxidizers will generate heat and cause fire.

Conditions to avoid: Avoid heat, sparks, flames, and all other sources of ignition.

Incompatible materials: Avoid oxidizing agents, acids and bases.

Hazardous decomposition products: Thermal decomposition may yield carbon oxides.

11. TOXICOLOGICAL INFORMATION

Acute effects of exposure:

Inhalation: Inhalation of vapors may cause minor irritation of the mucous membranes and upper respiratory tract and central nervous system effects such as dizziness, drowsiness and headache.

Ingestion: Swallowing may cause nervous system and gastrointestinal effects.

Skin contact: No adverse effects are expected. Minor irritation is possible. Therapeutic use has resulted in red, swollen, blistered or crusted skin.

Eye contact: Contact may cause mild irritation with redness and tearing.

Chronic Effects: None known.

Sensitization: Components are not known to be sensitizers. Allergic reactions are possible in sensitive individuals.

Germ Cell Mutagenicity: None of the components have been shown to cause germ cell mutagenicity. The mutagenic potential of tretinoin was evaluated in the Ames assay and in the in vivo mouse micronucleus assay, both of which were negative.

Reproductive Toxicity: In dermal fertility studies of tretinoin in rats, slight (not statistically significant) decreases in sperm count and motility were seen at 0.5 mg/kg/day, and slight (not statistically significant) increases in the number and percent of nonviable embryos in females treated with 0.25 mg/kg/day and above were observed. In oral studies in rats with tretinoin, decreased survival of neonates and growth retardation were observed at doses in excess of 2 mg/kg/day. Oral tretinoin has been shown to be teratogenic in rats, mice, hamsters, and subhuman primates. It was teratogenic and fetotoxic in Wistar rats when given orally or topically in doses greater than 1 mg/kg/day. However, variations in teratogenic doses among various strains of rats have been reported. In the cynomolgus monkey, which metabolically is closer to humans for tretinoin than the other species examined, fetal malformations were reported at doses of 10mg/kg/day or greater, but none were observed at 5 mg/kg/day, although increased skeletal variations were observed at all doses. A dose-related increase in embryoletality and abortion was reported. Similar results have also been reported in pigtail macaques. Topical tretinoin in animal teratogenicity tests has generated equivocal results. There is evidence for teratogenicity (shortened or kinked tail) of topical tretinoin in Wistar rats at doses greater than 1 mg/kg/day. Anomalies (humerus: short 13%, bent 6%, parietal incompletely ossified 14%) have also been reported when 10 mg/kg/day was topically applied. There are other reports in New Zealand White rabbits administered doses of greater than 0.2 mg/kg/day of an increased incidence of domed head and hydrocephaly, typical of retinoid-induced fetal malformations in this species. In contrast, several well-controlled animal studies have shown that dermally applied tretinoin may be fetotoxic, but not overly teratogenic in rats and rabbits at doses of 1.0 and 0.5 mg/kg/day, respectively. Topical tretinoin has been shown to be fetotoxic in rabbits when administered 0.5 mg/kg/day. Oral tretinoin has been shown to be fetotoxic, resulting in skeletal variations and increased intrauterine death in rats when administered 2.5 mg/kg/day. Ethanol is known to cause developmental toxicity when intentionally ingested during pregnancy.

Carcinogenicity: Ingestion of alcoholic beverages is known to cause cancer in humans (IARC group 1).

In a 91-week dermal study in which CD-1 mice were administered 0.017% and 0.035% formulations of tretinoin, cutaneous squamous cell carcinomas and papillomas in the treatment area were observed in some female mice. A dose-related incidence of liver tumors in male mice was observed at those same doses. The maximum systemic doses associated with the administered 0.017% and 0.035% formulations are 0.5 and 1.0 mg/kg/day, respectively. The biological significance of these findings is not clear because they occurred at doses that exceeded the dermal maximally tolerated dose (MTD) of tretinoin and because they were within the background natural occurrence rate for these tumors in this strain of mice. There was no evidence of carcinogenic potential when 0.025 mg/kg/day of tretinoin was administered topically to mice. None of the components are listed as carcinogens by IARC, NTP or OSHA.

Acute Toxicity Values: Acute Oral Toxicity Estimate (ATE) calculated: >5000 mg/kg
Tretinoin: Oral rat LD50 2,000 mg/kg
Ethanol: LD50 oral rat 7060 mg/kg; LC50 inhalation rat 20000 ppm/10 hr.
Propylene Glycol: LD50 oral rat 22,000 mg/kg, LD50 dermal rabbit >2000 mg/kg

12. ECOLOGICAL INFORMATION

Ecotoxicity values: No data is available
Persistence and degradability: No data is available
Bioaccumulative potential: No data is available
Mobility in soil: No data is available.
Other adverse effects: None known.

13. DISPOSAL CONSIDERATIONS

Dispose in accordance with all local, state and federal regulations. No specific disposal method is recommended.

14. TRANSPORT INFORMATION

	UN Number	Proper shipping name	Hazard Class	Packing Group	Environmental Hazard
DOT	UN1170	Ethanol Solution	3	II	No
TDG	UN1170	Ethanol Solution	3	II	No
IMDG	UN1170	Ethanol Solution	3	II	No
IATA	UN1170	Ethanol Solution	3	II	No

Transport in bulk (according to Annex II of MARPOL 73/78 and the IBC Code): Not applicable – product is transported only in packaged form.

Special precautions: None known.

15. REGULATORY INFORMATION

Safety, health, and environmental regulations specific for the product in question.

CERCLA: This product is not subject to CERCLA release reporting. Many states have more stringent release reporting requirements. Report spills as required under federal, state and local regulations.

SARA Hazard Category (311/312): Fire Hazard

EPA SARA 313: This product contains the following chemicals regulated under SARA Title III, section 313:
None

EPA TSCA Inventory: This product is a drug and not subject to TSCA.

CANADA:

Canadian CEPA: This product is a drug and not subject to CEPA regulations.

Canadian WHMIS Classification: Drugs are exempt from WHMIS

16. OTHER INFORMATION

NFPA Rating: Health = 1 Flammability = 3 Instability = 0
HMIS Rating: Health = 1* Flammability = 3 Physical Hazard = 0

SDS Revision History: Added Synonyms – 3W7, 7U8

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Disclaimer : This SDS has been prepared for occupational exposure. Consumers: Refer to the package insert or product label for appropriate consumer-specific information about this product when used according to manufacturer's directions. Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy of the information contained therein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequence of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s).